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Sakel Versus Meduna:

Different Strokes, Different Styles of Scientific Discovery

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Abstract

It is ironic that Laszlo Meduna and Manfred Sakel made epochal discoveries in psychiatry only two years apart because in most other ways, the two men could hardly be more different. The story of their differences and similarities invites us to consider the personal preconditions for scientific discovery. What common denominators led them to develop treatments, which represent the introduction of convulsive therapy, which remains today the most powerful treatment in psychiatry? Despite the marked differences in their personalities, Sakel and Meduna shared intellectual quickness, drive, and a willingness to take risks, three qualities that, in the case of these individuals at least, came together to revolutionize the treatment of serious psychiatric illness.

Keywords

insulin coma therapy; Laszlo Meduna; Metrazol convulsive therapy; Manfred Sakel; scientific discovery

It is ironic that Laszlo Meduna and Manfred Sakel, within two years of each other, made epochal discoveries in psychiatry because otherwise, the two men were as different as chalk and cheese. The story of their differences and similarities invites the question: What are the personal preconditions of scientific discovery?

Sakel and Meduna made their discoveries only two years apart, in 1933 and 1935. Shorter and Healy offer a larger context of these events.¹ On November 3, 1933, at a meeting of the Medical Society of Vienna, Sakel announced the discovery of a “new type of treatment for schizophrenics and patients with confused excitation.” It consisted of putting them into a series of insulin comas. Numbers were not mentioned but Sakel’s chief, Otto Pötzl, a professor of psychiatry in Vienna, confirmed the procedure to be of highest value.²

Meanwhile, in Budapest, Laszlo Meduna, a young assistant physician in the Brain Research Institute of Professor Karoly Schaffer, a noted advocate of the histological approach to psychiatry, was exploring the apparently inverse relationship between epilepsy and schizophrenia. Meduna published his first results in extenso, unlike Sakel’s 1-paragraph squib in 1935 in a medical weekly. In the 27-page article, “Studies on influencing the course

of schizophrenia through biological means, I: camphor and cardiazol convulsions,” replete with cases, in the distinguished *Comprehensive Journal of Neurology and Psychiatry*, Meduna explained that convulsive doses of camphor triggered convulsions that seemed to have a beneficial effect on patients with schizophrenia.³ Given Sakel’s view that convulsions were a troubling adverse effect of his insulin coma therapy, credit for introducing convulsive therapy into psychiatry, in a lasting and systematic way (an 18th-century English physician introduced camphor for therapeutic convulsions), belongs rightfully to Laszlo Meduna.

Yet both Sakel’s and Meduna’s treatments represented the introduction of biological approaches in psychiatry, and convulsive therapy remains today the most powerful treatment that psychiatry has to offer. As New York electrotherapist Lothar Kalinowsky, the éminence grise of electroconvulsive therapy (ECT) in the United States, later said, “It was the insulin treatment that made psychiatrists therapeutic-minded.”⁴

What may we say of Sakel and Meduna as individuals? What common denominators led them to creativity?

Both were of Jewish origin, although religion seems to have played little role in the lives of either of them. Sakel was born in 1900 as Menachen Sokol in the village of Nadvornaya in a part of Russian Poland then belonging to Austria.⁵ Of his family, virtually nothing is known save that his father, an observant Orthodox Jew, cut such an outlandish appearance (in Sakel’s eyes) that Sakel later refused to bring him to New York (M. Fink, personal communication with William Karlner, January 27, 2003). Sakel later put abroad that his “rabbinical family descended from the philosopher and physician Maimonides,”⁶ but this may have been one of the many fibs with which Sakel’s life was filled. After becoming wealthy in New York after his definitive migration in 1937, Sakel was later said to favor Zionist causes.⁷ His New York girlfriend was non-Jewish, and there is no record of his observance of Jewish holy days.

Meduna by contrast came from a family of conservative Sephardic Jews (of Mediterranean origin, in contrast to the Ashkenazic Jews of Eastern Europe such as Sakel). Born in 1896, he spent his high school years in a Catholic boarding school.⁸ Of his religious observance, little is known, but he kept his Jewishness sufficiently under wraps that Sakel considered Meduna part of an anti-Semitic conspiracy allied against him to prevent him from getting a Nobel Prize.⁹ The Jewishness of the two discoverers thus gave them little in common.

In their path to discovery, the two followed markedly different routes. Despite his subsequent statements of rigorously applying the scientific method, Sakel seems to have stumbled across insulin coma by accident. Sakel emphasized that the year of discovery of insulin’s benefits in psychosis had been 1927, yet the date may have been contrived to emphasize his primacy over the hated Meduna and is difficult to reconcile with known facts. Sakel graduated with a degree in medicine in Vienna in 1925 and went up to a psychiatric sanatorium in the Berlin suburb of Lichterfelde, the chief physician of which was Kurt Mendel. Although Sakel later claimed to have been chief physician, his name does not figure in any of the private clinic’s advertisements in these years, and it is implausible that 2 years out of medical school, he would have been entrusted with running this imposing operation,

which specialized in treating addictive disorders and the major psychiatric illnesses of the prominent of Berlin.

Sakel claimed to have begun his voyage of discovery with theoretically justified animal experiments, ending in May 1927 with the decision to move on to human subjects.¹⁰ The testimony of those who knew Sakel in those Berlin days tells a more haphazard story. Heinz Lehmann, then just beginning his psychiatric training in Berlin, once slept in the same room as Sakel and heard a bit of his story: “I got the impression then that he was a bit flaky. He got his idea when he was treating heroin addicts with insulin in Berlin to help them over their withdrawal symptoms. I don’t remember what his rationale was, but it calmed them down. Once, one of his addicts who was also schizophrenic, accidentally slipped into a hypoglycemic coma. Sakel was scared but brought him out of the coma quickly with an injection of glucose. To his amazement, the patient showed a considerable improvement of his schizophrenic symptoms. Sakel then wanted to use hypoglycemic coma as a treatment for schizophrenia.”¹¹ It must be said that the use of insulin, discovered in 1922, was by the late 1920s quite common in psychiatry,¹² and Sakel would have needed little inspiration to attempt it on a patient. The genius of Sakel’s discovery was that he observed a psychiatric adverse effect from insulin and decided to explore its meaning systematically.

Sakel first published on the insulin treatment of morphine addiction, without mentioning coma or psychosis, in 1930.¹³ Of his announcement in 1933 of the insulin cure for psychosis, he later claimed to have received attention in the main newspapers of Vienna and indeed Europe. “My official proposal to employ such dramatic shocks with convulsions as a therapy was (in 1933) immediately widely and sensationally publicized in the daily press at home and abroad.”¹⁴ This was a complete fabrication: There was not a whisper in the main Vienna dailies of his announcement at the Medical Society. Heather Dichter kindly undertook a systematic search of the Viennese press for this period and found no mention of this event. When Sakel made the claim, during the World Congress of Psychiatry in Paris in 1950, he seemed to have been in the grips of an almost manic fit of self-aggrandizement. On stage, Meduna refused to shake his hand and did not subsequently submit the text of his own lecture for publication.

The very opposite of Sakel in path to discovery, Meduna’s work was a model of the scientific method. In the late 1920s, he was more of a brain biologist than a psychiatrist, and in Schaffer’s Institute, he became intrigued by the finding of the proliferation of glial tissue in the brains of patients with epilepsy seen postmortem, in contrast to the absence of glia in the brains of patients with schizophrenia. He then read several epidemiological studies that demonstrated in asylum populations an absence of epilepsy, indeed in one institution, patients who had recovered from their schizophrenia after epileptic attacks. Meduna formed the question: Could there be an antagonism between epilepsy and schizophrenia? After undertaking preclinical experiments to establish safety, he contemplated the big wager: human trials. As he later said in his manuscript autobiography, “I believed that this antagonism should be utilized to cure not epilepsy, but schizophrenia.”¹⁵ Meduna set out to systematically administer a convulsive agent (first camphor, then a variety of convulsants, then finally pentylenetetrazol, sold in Europe as Cardiazol, in the United States as Metrazol) to patients with schizophrenia (many of whom apparently had catatonia, a happy diagnostic

confusion for Meduna because chronic psychosis yields to convulsive treatment, if at all, only after long and wearisome treatments, whereas catatonia responds at once). Meduna thus established a testable hypothesis on the basis of biological findings and demonstrated it with a proper clinical trial that, although lacking a placebo control group, showed substantial efficacy for cardiazol. Gazdag et al¹⁶ provide a systematic analysis of Meduna's early cases.

Finally, one can note the difference in how the two investigators dealt with their triumphs. Both became world famous. For Meduna, there was a steady string of visitors to Budapest that challenged his pocketbook in taking them all to dinner. In 1939, he emigrated to the United States, took a post in psychiatry first at Loyola University, then at the Illinois Psychiatric Institute of the University of Illinois, both in Chicago. To keep body and soul together, he had a modest private practice. In 1955, he wrote Ugo Cerletti, the originator of ECT, "Just as you, I was unable to save any of the money from the use of the shock treatments. In fact, I made no money at all with the Metrazol treatment inasmuch as I never had any private patients to whom I gave Metrazol treatment." ¹⁷

Meduna remained scientifically vital until his death in 1964, helped to found in 1953 the Society of Biological Psychiatry. He was involved with such innovative therapies as carbon dioxide treatment and with pioneering diagnoses such as oneirophrenia (dreamlike psychosis). Yet what is most interesting for our purposes is that as soon as a superior form of convulsive therapy came along, in the form of electroconvulsive treatment in 1938, he lost interest in chemical convulsive therapy. He saw it as inferior to initiating seizures electrically. He wrote to 1 correspondent in 1947 who had inquired about chemical convulsive therapy reprints: "You know this old convulsive therapy is past history for me and I believe for almost every psychiatrist. I do not believe the original publications have much value anymore." ¹⁸

Sakel by contrast clung tenaciously to insulin coma therapy until his death of a myocardial infarction at age 57. Sakel shunned institutional affiliations in New York, or perhaps it was his famous arrogance that discouraged colleagues at places such as New York University from approaching him (he did get a feeler from the New York State campus in Albany but apparently did not respond to this provincial quiver). For years, he took pains to rebuke Meduna (unfairly) for plagiarizing his own work and to insist on the danger of inducing fits, as opposed to healing comas. He opposed ECT for the same reason.¹⁹ Driven more by his jealousy of Meduna than any interest in historical accuracy, in 1947, Sakel maintained that it was he, Sakel, who had introduced metrazol convulsive treatment before realizing it was a bad idea! He made no mention of Meduna in advancing this claim. ⁸

In New York, Sakel lived in the Murray Hill Hotel on Park Avenue, receiving wealthy patients in his suite for insulin subcoma treatment: injecting homeopathic doses of insulin for which, in the recollection of William Karliner, his second cousin, he received enormous honoraria. He administered insulin coma therapy at the private Slocum clinic upriver in Beacon, New York, driven to and fro in the limousine of one of his private patients (E. Shorter and M. Fink, personal communication with William Karliner. 2004). Unlike Meduna, Sakel became very wealthy, acquiring a reputation among his contemporaries as driven by greed. As Kalinowsky, now in New York, wrote to his former colleague Lucio Bini

back in Rome in 1940 of Sakel, “He has the worst possible reputation as being a money-grubber [un affarista].”²⁰ And Meduna said a decade later of Sakel, “He is among the big money makers of our profession”. He has found private practice better suited to him than the somewhat sour honey of research.”²¹ At his death, Sakel left \$2 million to his friend Marianne Engländer²² and a well-endowed private foundation.²³

The point is not to rebuke Sakel for his apparent avarice or praise Meduna for his modesty and lack of materialism. Rather, it is that these were two totally different individuals, with psychological constitutions as diverse as could be. It is possible that Sakel had a touch of manic-depressive illness, for in addition to such moments of hyperdrive as his appearance at the World Congress of Psychiatry in Paris in 1950, he complained once privately to Joseph Wortis, explaining his tardiness in corresponding, “I was for certain private reasons in a small depression [in einem kleinen Tief].”²⁴

Yet, both Sakel and Meduna had the kind of active mind, the drive and the willingness to take risks that seem essential for the introduction of truly innovative treatments. These are three qualities that, in this pair of individuals at least, seem to have come together to produce innovation:

1. Natural intellectual quickness, in the sense of an ability to make lateral connections. Sakel immediately saw that an adverse effect could be converted to a therapeutic benefit; Meduna glimpsed therapeutic possibilities in the natural opposition of two disease conditions and responded to the therapeutic principle (on the table since Julius Wagner von Jauregg’s malarial fever cure of neurosyphilis in 1917) of treating a disease with a disease.
2. Natural energy. For Sakel, bestirring himself as a junior physician in an expensive private hospital conscious of its public image required drive. Coming out of the East European “shtetl” and full of drive, Sakel seized the moment. Meduna invested large amounts of private time in microscopy, animal work, and clinical trials. Again, he was an individual full of energy.
3. Willingness to take risks. By today’s standards, the risks both men ran were awesome. Putting treatments of singular dangerousness into patients and inducing comas and convulsions therapeutically required courage, to say the least. One can imagine the reactions of an institutional review board today. Today the work of these 2 pioneers would be inconceivable.

Sakel was single; Meduna’s wife was his secretary. Their work cost little, and, on the Central European academic model, they had few distractions in their lives save work. There are lessons for our own time in the lives of Sakel and Meduna, but they are not necessarily encouraging ones. The world of endless research grant applications, of navigating the pitfalls of ethics review boards, and of balancing the demands of home life and office do not encourage us to imagine that similar figures might spring forth soon.

Acknowledgments

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